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Progress over the last year on the development and utilization of the multineuronal data acquisition and control systems has been significant. Most of the hardware and software development has been completed, and further development has focussed on improving user interfaces, portability of the software, and on novel analysis strategies. Much of the research effort has now shifted to utilizing the patterned microwire arrays for neurophysiological recording during performance of a delayed match to sample task. Initial studies have produced some surprising results which indicate that neurons distributed throughout the various layers of the hippocampus encode a combination of positional, behavioral and mnemonic information during performance of the memory tasks. The accompanying report summarizes these and other accomplishments in the second year of the award.

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Multiple Neuron Recording in the Hippocampus of Freely Moving Animals

Progress Report for AFOSR-90-0092

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Progress Report

Summary

Progress has been significant over the previous year on the development of multineuronal recording and systems for analysis of the multineuronal data. This was a primary objective of the three laboratory consortium, and it has been a principle focus of the research efforts. The multitasking computer system has been in operation in all three laboratories this past year, as well as the DSP-based multineuron spike-sorter and the associated software interface for neural spike discrimination. Much of the research effort in the past year has been directed toward implementing the spike-sorter system, collecting multineuron data, and developing the analysis strategies. In addition, studies using the multineuron data acquisition have revealed new relationships between the behavioral events in the DMTS and patterns of simultaneously active neurons in the hippocampus. The following report will summarize these and other accomplishments in the third year of the award.

Research Objectives: Statement of Work

The research objectives of the third year ot the award were primarily: (1) to continue to implement the computer system for behavioral control and multiple neuron recording in hippocampus and related structures, and (2) to utilize these techniques in sample memory tasks to determine the nature of sensory processing by the hippocampus and related structures. Each of these objectives will be dealt with in a separate section below.

Multineuron Recording System: The first two years of the project were dedicated to development of the multineuron data acquisition and behavioral control computers. The multiuser Motorola Delta 2616 is now capable of simultaneous control of up to 8 experimental chambers, with synchronous or asynchronous recording of up to 64 channels of electrophysiological data per chamber. Each of the experiments can now be controlled from one console terminal or separate terminals, with online reports of behavioral variables and graphic display of the electrophysiology. Software control of the programs has been expanded to include a wide variety of training programs, operator alerts when specific sequences of behavioral events occur, and direct output of data to spreadsheet format for offline analysis.

A second development of this phase of the project was the translation of all Motorola-based analysis programs to machine-independent C-language programs. A principal benefit of the translation was the adaptation of Dr. J. Chapin's ANALYZE program to the Intel 80x86/MS-DOS "PC" computers, greatly increasing the speed and capacity of the analysis. The translation of analysis programs is now complete and has been delivered to all three laboratories. Several customized programs have been developed (one of which will be discussed in the progress report below) which have provided new perspectives for examining the multineuron data. Continued development of analysis programs, as well as adaptation to MS-Windows, and Windows-NT operating systems is currently in progress. The combination of these programs makes this an extremely powerful and portable laboratory research package for analyzing the volume of physiological data which can now be recorded with the multineuron recording system.

The third focus of development for this time period has been the continued refinement of the DSP-based spike sorter programs. The MS-Windows control software has been expanded to include multiple window discriminator functions, principal components analysis, cluster-cutting, activity meters, strip charts, firing rate histograms and on-screen template matching for neural spike selection. The spike-sorter instrumentation currently in use in the laboratory can now be configured to allow the 128 electrode inputs and 64 discriminator outputs to be independently assigned on one or more experimental chambers (to a maximum or 4) with independent control of the spike sorter criteria for each experiment. In combination with the patterned microwire arrays, the multichannel electrophysiological data has revealed startling new data on information processing in the hippocampus during the delayed memory experiments currently in progress in the laboratory.

Personnel:

Dr. Robert Hampson, Ph.D. Research Asst. Professor BGSM.
Mr. Terrence Bunn, Advanced Systems Programmer

Information Processing and Delayed Memory Studies, Phase III: Progress to date on these experiments has concentrated on correlation of behavioral events with the neural activity recorded in the hippocampus during performance of these tasks. Several publications are currently in press or in preparation from these experiments and are listed on the last page. A brief summary of the findings from each study will be presented below.

Tone Signal Detection and Discrimination Task: Progress on this phase of the project has concentrated on analyses of the hippocampal and cortical tone-evoked neural activity from the auditory signal detection and discrimination task. In particular the analysis has focussed on the transmission of information between dentate gyrus and neocortex, and the recurrent feedback of this information onto hippocampal inputs to modify hippocampal excitation on subsequent trials. The sequential dependency previously observed in auditory evoked potentials and tone-evoked signle neuron discharges would thus reflect modulation of hippocampal inputs to maintain neural activity within an optimal range for processing the information represented by the input. The possible anatomic basis for this feedback is currently being investigated by a combination of multineuron recording and selective hippocampal lesions. Completion of this study will utilize multineuron recording from sites in hippocampus, entorhinal cortex and perirhinal cortex to monitor the likely functional connections involved in the information processing loop. A neural network model is currently under development based on the initial findings, and will be refined using the data obtained from the planned experiments.

Delayed Match to Sample Memory Task: The extensive analysis of single hippocampal neuron activity in the DMTS task has been reported in two publications completed in the last year. The analysis identified specific interactions of behavioral and spatial factors which influence the activity of hippocampal CA1 and CA3 complex spike cells. Numerous conjunctive influences on neural firing have been identified, including: phase of the DMTS task, lever position, and length of the delay interval. The identified response patterns suggest that combined activity of the cell types is sufficient to fully encode all features of the DMTS task. In addition, these results indicate that hippocampal neural activity does not represent purely spatial, nor purely mnemonic information, but a combination of positional and task-specific factors.

Implementation of multineuron data acquisition in the DMTS task has resulted in several novel findings. Initial experiments utilized patterned arrays of microwire electrodes with pairs of electrodes simultaneously positioned in the CA3 and CA1 layers of the hippocampus. The original goal of these experiments was to identify correlated neural activity in the two layers indicative of functional anatomic projections from CA3 to CA1. The cross-correlation analyses required quite large datasets due to the large number of neural spikes required (>1000 spikes/channel), vs the relatively low firing rate of the complex spike cells (<5/sec). Acquisition and analysis of this dat is currently in progress. To facilitate analysis of the data, an online rate display program (ORDisp) was developed by Mr. Bunn to display the multineuron activity as a sequence of colored-coded firing patterns synchronized to behavioral events. A surprising result of this analysis was the finding that particular patterns of neural firing distributed across the CA3 and CA1 cell fields were repeated for subsequent behavioral events, but not at other times during the session. These spatiotemporal patterns reinforce the finding of conjunctive coding of spatial <u>and</u> task-relevant information in the hippocampus *during* behavior. These data are currently being analyzed and will be prepared for publication during the next year.

Personnel:

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Mr. M. Todd Kirby, Graduate Student Technician, BGSM
Ms. Gina C. King, Research Technician III, BGSM

Publications and Presentations Relevant to This Grant

Heyser CJ, Hampson RE, Deadwyler SA. The effects of delta-9-THC on delayed match to sample performance in rats: Alterations in short-term memory produced by changes in task specific firing of hippocampal neurons. *J.Pharmacol.exp.Ther.* **264**:294-307,1993.

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